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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/070,647	06/18/2002	Merton Bernfield	701039-048929	9224

7590 01/13/2004

EXAMINER
GRASER, JENNIFER E

ART UNIT	PAPER NUMBER
1645	

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DATE MAILED: 01/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/070,647	BERNFIELD ET AL.	
	Examiner	Art Unit	
	Jennifer E. Graser	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *11 and 12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 6/18/02 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6/18/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restriction

1. Applicant's election without traverse of Group I, claims 1-10, in the paper filed on 10/31/2003 is acknowledged. Claims 11 and 12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

Specification

2. The disclosure is objected to because of the following informalities:

In the 'Brief Description of Drawings' on page 8, line 11 of the specification, 'Figure 2" should be changed to 'Figures 2A and 2B".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite due to the term "syndecan-1 decoys". It is unclear what is encompassed by this language. The metes and bounds of the invention cannot be understood. It is also unclear what is encompassed by the term "bacterial factor responsible for syndecan-1

cleavage". The only known bacterial factor responsible for syndecan-1 cleavage is Las-A protein from *P.aeruginosa.* Do applicants intend for the scope of this language to include more than Las-A? If so, what other factors are encompassed?

Claim 1 is also vague and confusing because it recites steps a) and b), but then recites (a), (b) and (c) later in the claim. A semicolon after the word 'from' and removal of the parentheticals would help clarify the claim.

Claim 5 is vague and indefinite because it recites that the protein kinase inhibitor may be 'genistein'; however, the claims for which it depends (claim 1) specifically states that the inhibitor cannot be 'genistein'. Correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the

state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The claims are directed to a method of treating a bacterial infection comprising: a) determining whether the bacterium causing the infection is capable of enhancing host cell syndecan-l shedding; b) administering an effective amount of a compound that inhibits syndecan-1 shedding to a subject suffering from said infection, wherein the compound is selected from from (a) inhibitors of a bacterial factor responsible for syndecan-l cleavage, (b) compounds that bind the syndecan and disrupt cleavage, © syndecan-l decoys, and (d) inhibitors of the host cell shedding mechanism, except when the bacterium is *Pseudomonas aeruginosa*, the compound is not genistein or tyrphostin A47. However, specification provides no evidence that such a method could treat any bacterial infection.

There is no reported association between syndecan-1 shedding and bacterial infection in the prior art and the instant specification has not established that the two have a clear association. Augmentation of shedding in some bacterial pathogens has been shown in the prior art; however this has not been correlated to bacterial infection and the responsible shedding enhancers have not been identified. Additionally, the instant claims are drawn to treating *any* bacterial infection by using a bacterial factor responsible for syndecan-1 cleavage from *any* bacteria. It is known that shedding is not augmented in many bacterial pathogens. Further, the prior art has not

identified any bacterial factors responsible for syndecan-1 shedding, with the exception of the Las-A protein. The specification at the top of page 21 teaches that several Gram positive and Gram negative bacteria do not enhance shedding of syndecan-1. The specification has identified the Las-A protein from *P.aeruginosa* as a bacterial factor responsible for syndecan-1 shedding, but has failed to identify any other bacterial factors responsible for syndecan-1 shedding from any other bacteria. A shedding enhancer has not been identified in *S.aureus*. Accordingly, the agents to be used in parts (a), with the exception of inhibitors of the Las-A protein of *P.aeruginosa*, have not yet been identified. Accordingly, it would take one of skill in the art undue experimentation to identify other agents which could be used to inhibit a bacterial factor respsonsible syndecan-1 shedding. Genentech Inc. v. Novo Nordisk A/S (CAFC) 42 USPQ2d 1001 clearly states: "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. See Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.") Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. The specification fails to identify any specific 'syndecan-1 decoys', inhibitors of the host cell shedding mechanism, or inhibitors of a bacterial factor responsible for syndecan-1 cleavage, with

the exception of inhibitors of the Las-A protein of *P.aeruginosa,* much less show that these factors possess the ability to treat *any* bacterial infection. Accordingly, the broad scope of the claims is not enabled.

The specification provides no results that administering a compound selected from any one of (a) inhibitors of a bacterial factor responsible for syndecan-l cleavage, (b) compounds that bind the syndecan and disrupt cleavage, © syndecan-l decoys, and (d) inhibitors of the host cell shedding mechanism will treat a bacterial infection. Bacterial pathogens are extremely complex and use many different factors to cause infection and disease in a host. The specification has not shown that the claimed method can treat a bacterial infection. Claim 10 recites that the bacterial infection may be one of the respiratory system, the urinary tract, the skin, the eye, or the bloodstream. No enabling disclosure is provided for such a claim.

The specification has demonstrated that Las-A is the shedding enhancer of *P.aeruginosa.* The specification has demonstrated that BB1101 and Tyrphostin A25 can inhibit both purified Las-A and *P.aeruginosa* supernatant-enhanced syndecan-1 shedding by more that 70% and 60%, respectively. Accordingly, methods of inhibiting enhanced syndecan-1 shedding caused by *P.aeruginosa* by administering BB1101 or Tyrphostin A25 are enabled by the instant specification. The specification has also provided results in Table 2 and Example 2, and pages 30-32, *P.aeruginosa*-enhanced shedding of syndecan-1 promotes lung infection by this pathogen and that administration of BB1101 can treat this type of lung infection. However, there are no results which demonstrate that an antibody to Las-A or any other inhibitor of the protein, itself,

can treat a bacterial infection. The results only show that compounds which have been known in the art to inhibit syndecan-1 shedding can also be used to inhibit syndecan-1 shedding that is enhanced due to the Las-A protein. Specific evidences must be provided that demonstrate that an actual inhibitor of the Las-A protein, not of general syndecan shedding, can inhibit syndecan-1 shedding and treat *P.aeruginosa* infection in order to enable this additional scope of treating *P.aeruginosa* lung infection. The extremely broad scope of the instant claims is not enabled.

In the instant case, the nature of the invention is preventing *any* bacterial infection, (2) the prior art teaches that treating bacterial infection, particularly *P.aeruginosa* lung infection, is difficult. Although the level of skill of those in the art (7) is high, (3) the art is highly unpredictable, (8) the breadth of the claims is extremely broad, (6) and the quantity of experimentation, is undue. The specification provides a limited working example to a much narrower scope, i.e., that compounds which have been known in the art to inhibit syndecan-1 shedding can also be used to inhibit syndecan-1 shedding that is enhanced due to the Las-A protein.

7. Correspondence regarding this application should be directed to Group Art Unit 1645. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1645 Fax number is (703) 872-9306 which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (703) 308-1742. The examiner can normally be reached on Monday-Friday from 7:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

J Graser 1/7/04

JENNIFER E. GRASER
PRIMARY EXAMINER